

S/N 10/089,431

PATENTREMARKS

Applicants respectfully request reconsideration of the present case in view of the above amendments and the following remarks.

Claims 1, 2, 6, 8-12, 16, 18-21, 25, 27 and 28 are currently pending. Claims 1, 11, and 21 have been amended. No new matter has been inserted. Support for the amendment of claim 1, 11, and 21, can be found in the specification at least in table 1 on page 11.

35 U.S.C. § 103(a)

Claims 1, 2, 6, 8-12, 16, 18-21, 25, 27 and 28 were rejected under 35 U.S.C. § 103(a) over Duerer et al. (USPN 5,869,086), Godbey (USPN 6,086,911) and Fukiage et al. (EP 0 771 565). Applicants respectfully traverse this rejection.

The Examiner indicated that the burden was shifted to the Applicants to provide unexpected results that would lend patentable weight to the limitations of the claims. Further, the Examiner has alleged that the results shown in the specification from the combination of isopropyl myristate and polyoxyethylene oleyl exhibit a merely additive effect.

In reply, Applicants point out that claims 1, 11, and 21 now feature "20 W/W% of polyoxyethylene oleyl ether" and further assert that the claimed amount of polyoxyethylene oleyl ether exhibits a surprising result that is not merely additive.

In the specification, the data on cumulative drug amounts transferred are presented at pages 16-17, Tables 3-5. The data is summarized in the following tables for ease of comparison among them. Table #1 shows cumulative drug amounts transferred in 36 hours with transdermal patches using a single enhancer (either EAO or IPM).

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PATENT**Table #1**

| Transdermal Patch No. | Cumulative Amount Transferred in 36 hrs ($\mu\text{g}/\text{cm}^2$) |
|------------------------------|---|
| P7 (10% EAO) | 42.83 |
| P8 (20% EAO) | 64.74 |
| P9 (10% IPM) | 4.14 |
| P10 (20% IPM) | 7.66 |

EAO = EAC9995 (polyoxyethylene oleyl ether)

IPM = isopropyl myristate

Applicants draw the Examiner's attention to the data for 10% EAO (P7) and 20% EAO (P8). In the absence of any amount of IPM, doubling the amount of EAO (e.g., 20% vs. 10% EAO) only yielded roughly a 1.5 fold increase in the amount of drug transferred (e.g., 64.74 vs. 42.83). Thus, doubling the amount of EAO in the absence of IPM fails to even yield additive effects on the amount of drug transferred. This data makes the results shown in Table #2 very unexpected and surprising.

Table #2 shows the actual cumulative drug amount transferred in 36 hours using combinations of EAO and IPM. Table #2 also shows the cumulative amount of drug transferred in 36 hours that would be expected based on the data presented in Table #1 and assuming additive effects.

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PATENTTable #2

| Transdermal Patch No. | <u>EXPECTED</u> Cumulative Amount Transferred in 36 hrs (ug/cm²) | <u>ACTUAL</u> Cumulative Amount Transferred in 36 hrs (ug/cm²) | Ratio Between Actual/Expected |
|------------------------------|--|--|--|
| P2 (10% EAO + 10% IPM) | P7+P9 = 46.97 | 59.92 | 1.276 |
| P3 (10% EAO + 20% IPM) | P7+P10 = 50.49 | 77.53 | 1.536 |
| P4 (20% EAO + 10% IPM) | P8+P9 = 68.88 | 166.61 | 2.419 |
| P5 (20% EAO + 20% IPM) | P8+P10 = 72.40 | 316.72 | 4.375 |

EAO = EAC9995 (polyoxyethylene oleyl ether)

IPM = isopropyl myristate

Table #2 clearly demonstrates that the use of 20% EAO along with an amount of IPM yields surprising results that are not merely additive. Specifically, Table #2 shows that the cumulative amount of drug transferred with patches P4 and P5 (both containing 20% EAO in combination with an amount of IPM) are 2.419 and 4.375 times higher, respectively, than what would be expected if the effect was merely additive.

This enhancement in drug transfer is even more remarkable in light of the data in Table #1 showing that doubling the amount of EAO (e.g., 20% vs. 10% EAO) in the absence of any IPM only yields a ≈ 1.5 fold increase in the amount of drug transferred. Therefore, the use of 20% EAO in combination with 10-20% IPM yields a remarkable enhancement in the amount of drug transferred that is not taught or suggested by the combination of Duerer, Godbey, and Fukiage. Moreover, the combination of Duerer, Godbey, and Fukiage fail to provide any reasonable expectation of success in achieving such a remarkable enhancement by the use of the specific combination of the enhancers as featured in claims 1, 11, and 21.

For at least these reasons, Applicants assert that they have carried the burden of showing an unexpected result and further assert that the combination of Duerer, Godbey, and Fukiage fail

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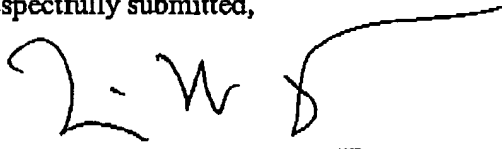
to render claims 1, 11, or 21 obvious. As claims 2, 6, and 8-10 are dependent on claim 1, claims 12, 16, and 18-20 are dependent on claim 11, and claims 25, and 27-28 are dependent on claim 21, they are also not rendered obvious by the combination of Duerer, Godbey, and Fukiage. Applicants respectfully request that this rejection be withdrawn.

Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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Date



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